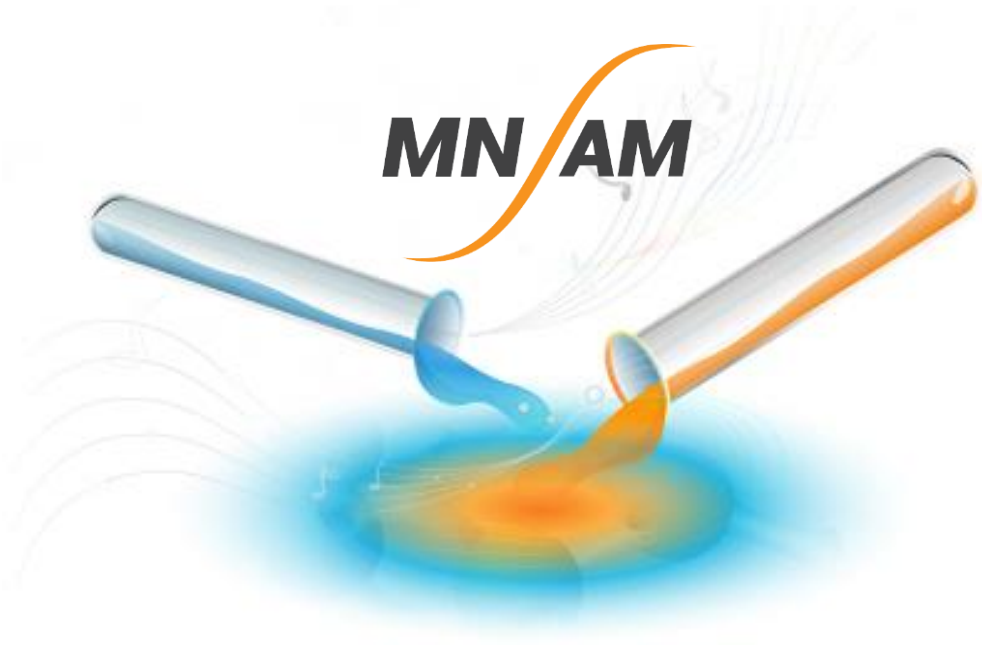
ChemTunes·ToxGPS®

Database and Knowledgebase for
Safety Evaluation and Risk Assessment



www.mn-am.com

ChemTunes·ToxGPS®

Data Mining & Retrieval

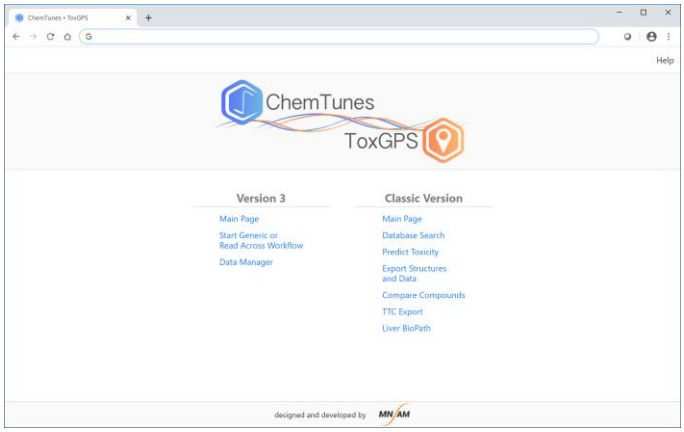
ChemTunes

- Chemoinformatics platform providing toxicity, safety evaluation and metabolism information
- Nearly 100,000 compounds with over 30,000 studies covering more than 70 endpoints

Data on Toxicity, Safety & Metabolism

Analogs & Profiles

Prediction, Workflows & Assessment



Human Health Endpoints

- Wide variety of endpoints important for safety assessment related to human health
- Data from toxicity and safety assessment databases, as well as *in silico* predictions

ChemTunes & ToxGPS

Genetic toxicity

- Bacterial reverse mutagenesis
- *In vitro* chromosome aberration
- *In vivo* micronucleus

Dermal toxicity

- Skin irritation
- Skin sensitization (hazard, potency)

Carcinogenicity

- Mouse tumorigenicity
- Rat tumorigenicity

Hepatotoxicity

- Steatosis
- Mitochondrial toxicity
- Human DILI

DART

- Pregnancy loss (rat, mouse, rabbit)
- Cleft palate (rat, mouse, rabbit)

Liver BioPath

- Metabolic reaction pathways
- Prioritized metabolites

Safety Evaluation…

- NOAEL/LOAEL, MOS, MOE, TDI, ADI, *etc.*

[1] Rathman JF, *et al.* Uncertainty Estimation and Quantitative Combination-of-Evidence using Dempster-Shafer Theory. *Comp. Tox.* **2018**, *6*, 16-31

[2] Cherkasov A, *et al.* QSAR modeling: where have you been? Where are you going to? *J. Med. Chem.* **2014**, *57(12)*, 4977-5010

[3] Leist M, Yang C, *et al.* Novel Technologies and an Overall Strategy to Allow Hazard Assessment and Risk Prediction of Chemicals, Cosmetics, and Drugs with Animal-Free Methods. *Altex* **2012**, *29, 4/12*, 373-388

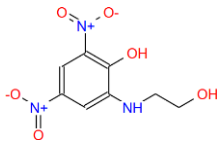
[4] Yang C, *et al*. Computational Toxicology Approaches at the US Food and Drug Administration. *ATLA* **2009**, *37*, 523-531

ToxGPS® – Prediction

- Knowledgebase for compound location, MoA QSAR & rule-based toxicity prediction and metabolism
- *In silico* safety assessment workflows including Read-Across and Threshold of Toxicological Concern

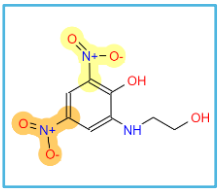
Prediction for Bacterial Reverse Mutagenesis

Prediction Results for compound #1



In database:	Yes
CHEMTUNES ID:	CMS-62110
Name:	2-Hydroximethyl picramic acid
Registry number(s):	99610-72-7
# studies in CHEMTUNES:	9

Overall prediction	Positive probability 0.99	
QSAR Model	**Positive probability**	
Global	0.58-0.85	
MoA Models		
Aromatic amine	0.39-0.65	
Aromatic nitro	0.38-0.61	
Phenol	0.54-0.84	

Chemotype alert	Chemotype alert match	Alert name	Odds ratio
		Aromatic nitro	6.02

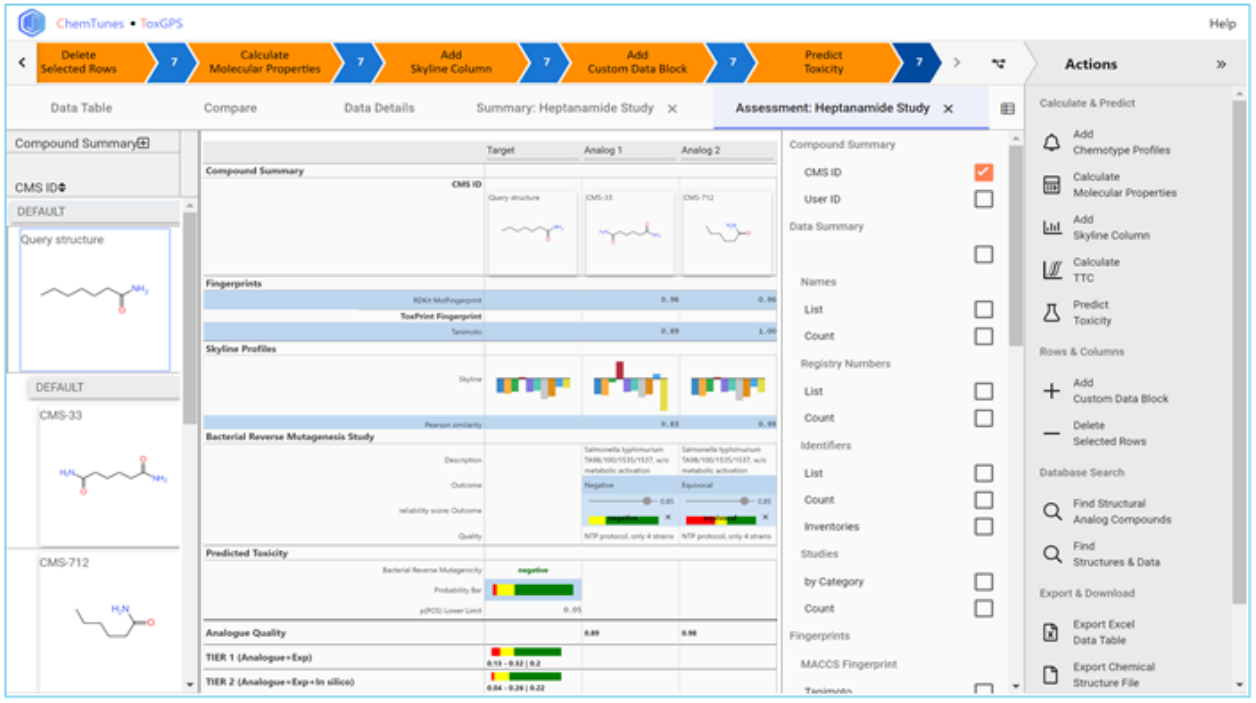
Combined Outcome

QSAR (global and MoA) as well as rule-based results are combined into one final outcome by a rigorous decision theory approach[1]

ToxGPS® – Read-Across

- Chemical speciation – metabolites and tautomers
- Generate analogues (structure-, property- and biology-based)
- Line up evidence
- Combine evidence for outcome and uncertainty estimation

Relevant
Reliable
Consistent
Reproducible



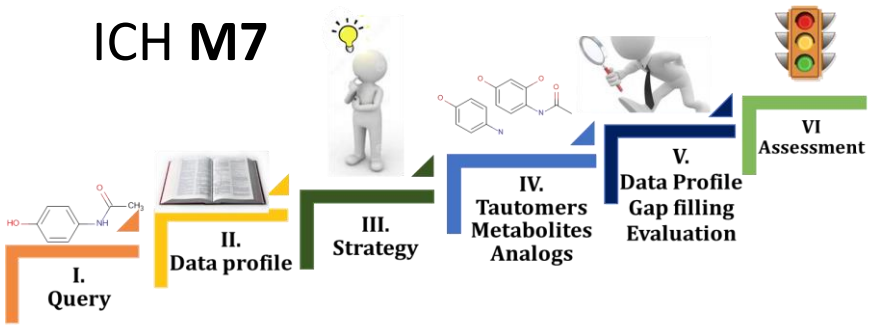
Inspiring Chemical Discovery
Navigating Chemical Safety
Empowering Knowledge

Marquee Features

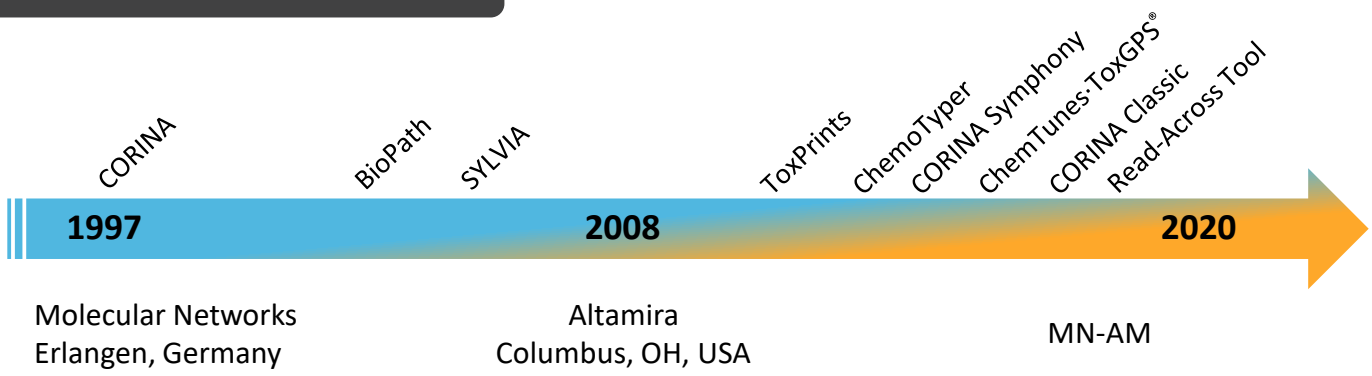
- Mechanism-based (MoA) QSAR models
- Rule-based and endpoint specific alerts[2,3]
- Proven approach used at US FDA for risk assessment[3,4]
- Data- and knowledge-based system
- Established chemoinformatics methods
- Decision theory approach[1]
- Weight-of-evidence (WoE) outcome and uncertainty[1]

Applications

- Compound location service
- Platform for *in silico* safety assessment
- Read-Across workflow
- ICH M7 genotoxic impurities in drug products
- TTC workflow
- Chemotype profiles and alerts
- Pairwise comparison of analog compounds



MN-AM at a Glance



Contact Us

German Office: Neumeyerstraße 28, 90411 Nuremberg, Germany Phone +49 (0)911 597 424 00
US Office: 1455 Candlewood Drive, Columbus, OH 43235, USA Phone +1 614 824 4586
www.mn-am.com info@mn-am.com